Derivation of qualitative dynamical models from biochemical networks

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2. Case studies
3. Trace semantics
4. Derivation of a coarse-grained qualitative semantics
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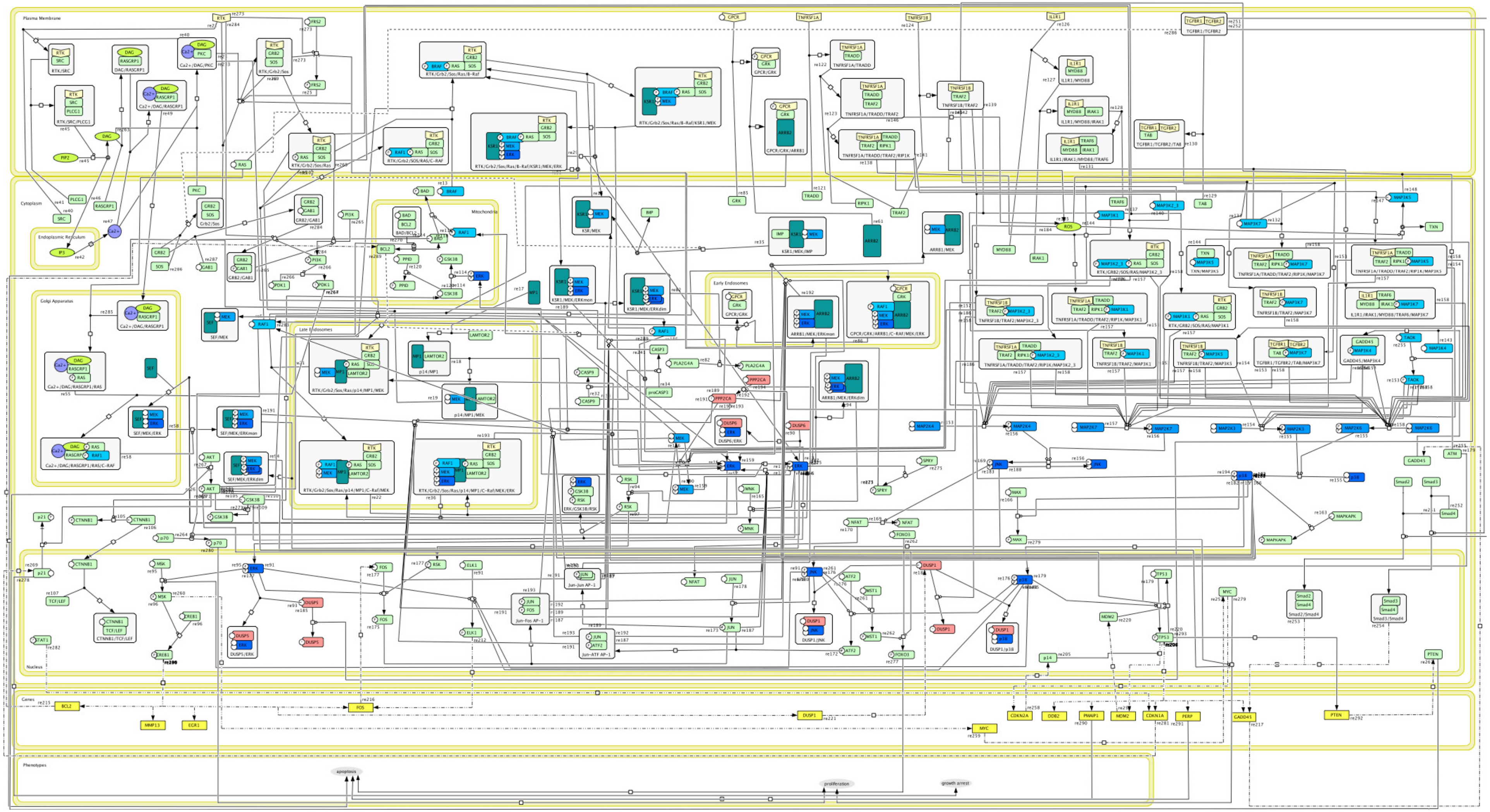
Aim and motivation

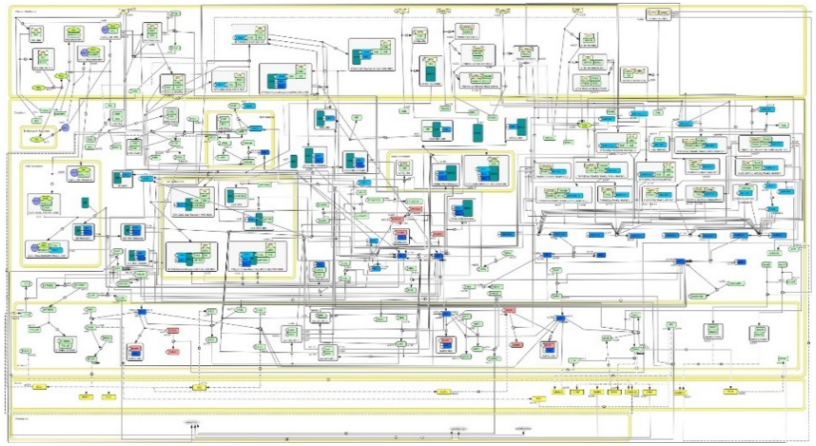
Molecular interaction map representing the MAPK network (involved in cell decision)



Grieco et al., *PloS Comp Biol*, 2013

Aim and motivation

Detailed molecular maps



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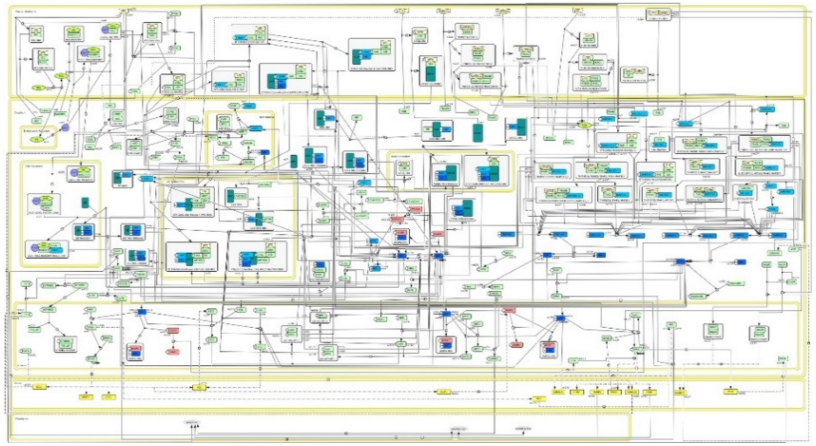
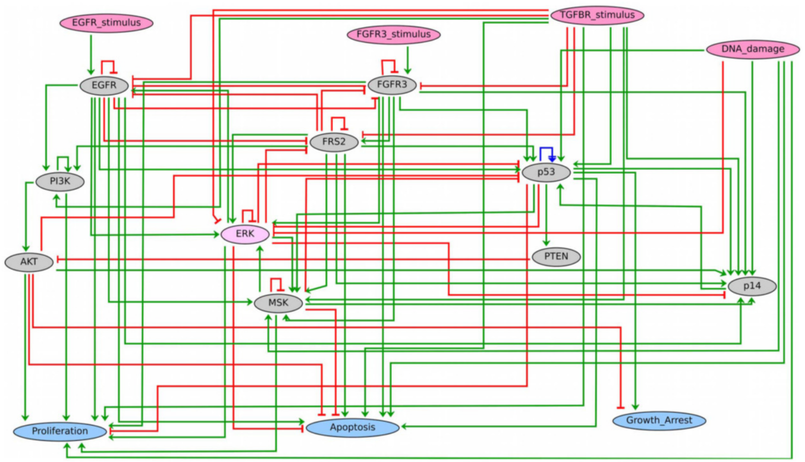


Coarse-grained dynamical models



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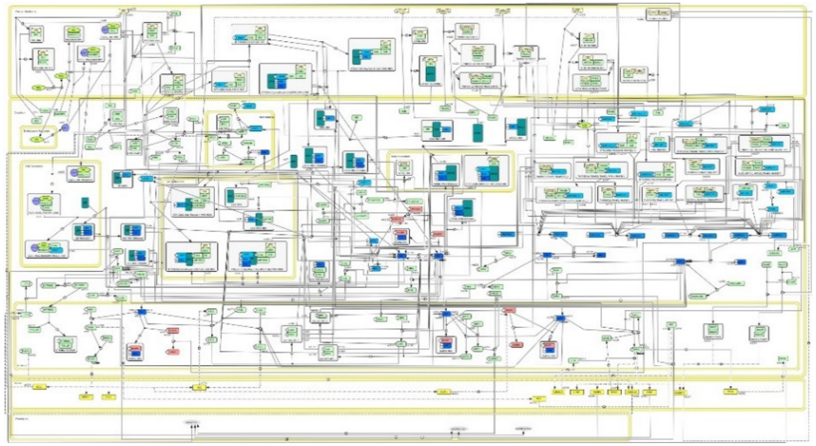
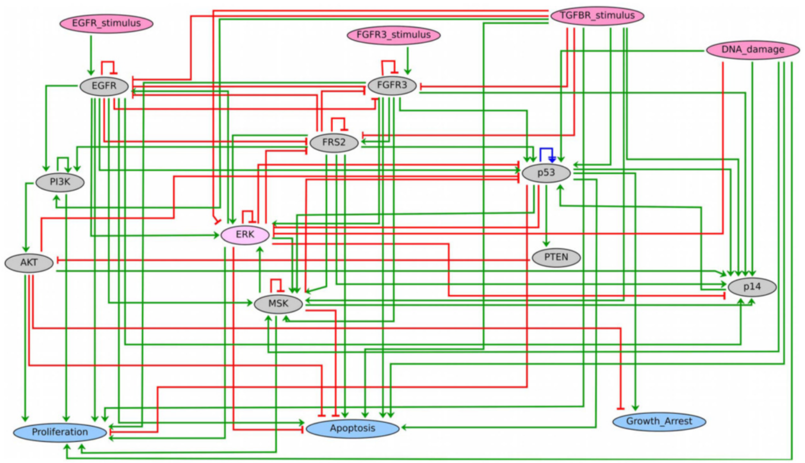


Automatic

Formal

Coarse-grained dynamical models



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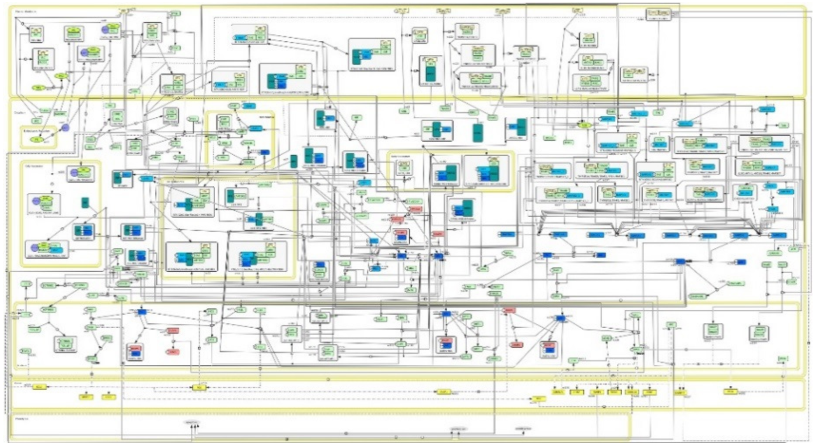
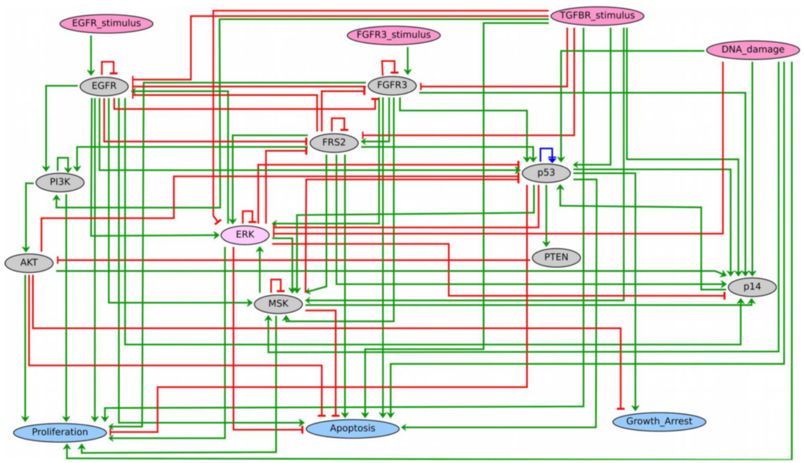


Abstract interpretation

Automatic

Formal

Coarse-grained dynamical models



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Case studies

Two case studies showing properties of interest

- A biochemical network showing a sequestration effect of a resource

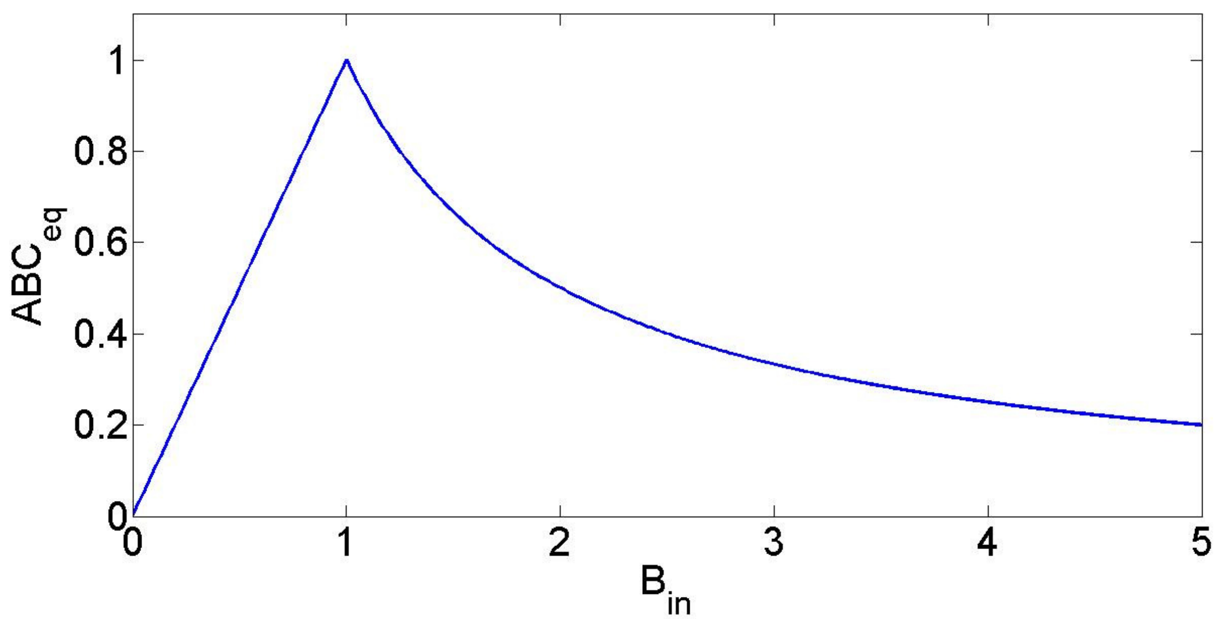
- A biochemical network showing a race between unary and binary reactions

A case study showing a sequestration effect

- Reaction scheme:

$$\begin{cases} A + B \xrightarrow{k_1} AB \\ B + C \xrightarrow{k_2} BC \\ A + BC \xrightarrow{k_1} ABC \\ AB + C \xrightarrow{k_2} ABC \end{cases}$$

- Analytic solutions (ODE's)



k1=k2=1

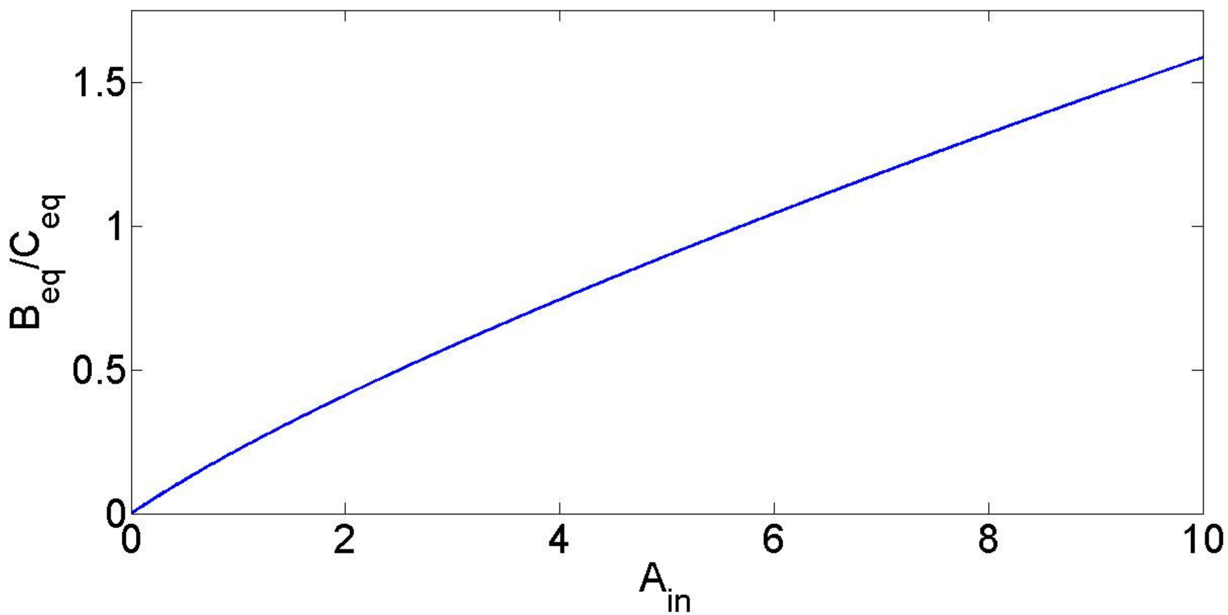
Ain=Cin=1
Abin=Bcin=ABCin=0

A case showing a race between unary and binary reactions

- Reaction scheme

$$\begin{cases} 2A \overset{k_1}{\rightarrow} B \\ A \overset{k_2}{\rightarrow} C \end{cases}$$

- Analytic solution (ODE's)



k1=k2=1

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Aim and method

- **Aim:** derivation of qualitative dynamical models from reaction networks which capture the salient properties of these two case studies

- **Method:** abstract interpretation framework for the formalisation of properties

Reaction network

- **Definition**

A network R of n reactions is a pair $(\nu, (M_r, V_r)_{1 \le r \le n})$, *where:*
(i) ν *is a set of chemical species;*
(ii) for each integer r *between* 1 *and* n,
(a) $M_r : \nu \longrightarrow \mathbb{N}$ *is a multi-set of chemical species,*
(b) and $V_r : \nu \longrightarrow \mathbb{Z}$ *is a reaction vector, such that* $M_r(x) + V_r(x) \ge 0$ *for any* $x \in \nu$.

- **An example**

$$\begin{cases} 2A \overset{k_1}{\to} B \quad (r1) \\ A \overset{k_2}{\to} C \quad (r2) \end{cases}$$

- $\nu = (A, B, C)$
- $V_{r1}(A) = -2$, $V_{r1}(B) = 1$, $V_{r1}(C) = 0$
- $M_{r1}(A) = 2$, $M_{r1}(B) = 0$, $M_{r1}(C) = 0$
- $V_{r2}(A) = -1$, $V_{r2}(B) = 0$, $V_{r2}(C) = 1$
- $M_{r2}(A) = 1$, $M_{r2}(B) = 0$, $M_{r2}(C) = 0$

Trace semantics

- **Transition system**

A reaction network $R \triangleq (\nu, (M_r, V_r)_{1 \leq r \leq n})$ *induces a transition system* $(\mathcal{Q}_R, T_R)$ *where:*
(1) $\mathcal{Q}_R$ *is the set* $\mathbb{N}^\nu$ *of the functions between* ν *and* $\mathbb{N}$*;*
(2) T_R *is the subset of* $\mathbb{N}^\nu \times [\![1, n]\!] \times \mathbb{N}^\nu$ *that contains all the triple* (q, r, q') *such that, for all chemical species* $x \in \nu$*:*
(a) $M_r(x) \leq q(x)$
(b) $q'(x) = q(x) + V_r(x)$.

- **Pretraces**

For any two sets A and Σ, a pretrace of elements of A and labels in Σ is an element of the set $A \times (A \times \Sigma \times A)^\star$.

Trace semantics

- **Trace**

A trace is a pretrace such that $(a'_0, (a_i, \lambda_i, a'_i)_{1 \leq i \leq k})$ such that $a_i = a'_{i-1}$ for any integer i between 1 and k.

- **Trace semantics**

The set of traces that is induced by a reaction network $R \triangleq (\nu, (M_r, V_r)_{1 \leq r \leq n})$ *and a set of initial states* $\mathcal{Q}_{R,0} \subseteq \mathcal{Q}_R$ *is defined as the set of the pretraces* $(q'_0, (q_i, r_i, q'_i)_{1 \leq i \leq k})$ *in* $\mathcal{Q}_R \times T_R^\star$ *such that:*

(1) first$(\tau) \in \mathcal{Q}_{R,0}$

(2) τ *is a trace of elements of* $\mathcal{Q}_R$ *with labels in* $[\![1, n]\!]$.

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- **Trace semantics expressed as the least fixpoint of a monotonic function**

$$\mathbb{F}_{\mathcal{Q}_{R,0}} : \begin{cases} \wp(\mathcal{Q}_R \times T_R^\star) \longrightarrow \wp(\mathcal{Q}_R \times T_R^\star) \\ \qquad\qquad X \longmapsto \mathcal{Q}_{R,0} \cup \{\tau \frown (q, r, q') \mid \tau \in X \ \wedge \ (q, r, q') \in T_R \ \wedge \ q = \mathit{final}(\tau)\} \end{cases}$$

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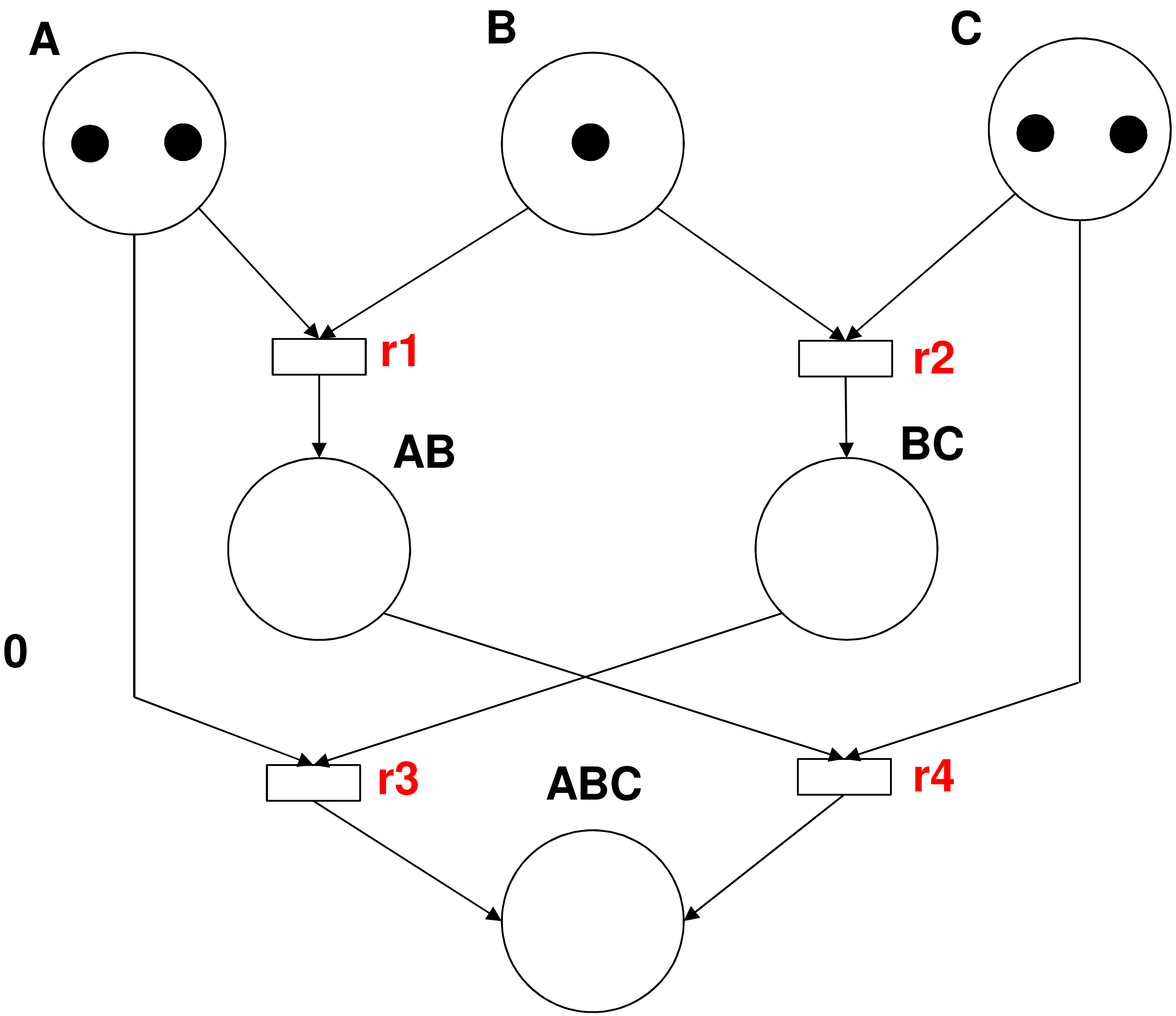
$$\mathit{lfp}\, \mathbb{F}_{\mathcal{Q}_{R,0}} = \mathcal{T}_{R,\mathcal{Q}_{R,0}}$$

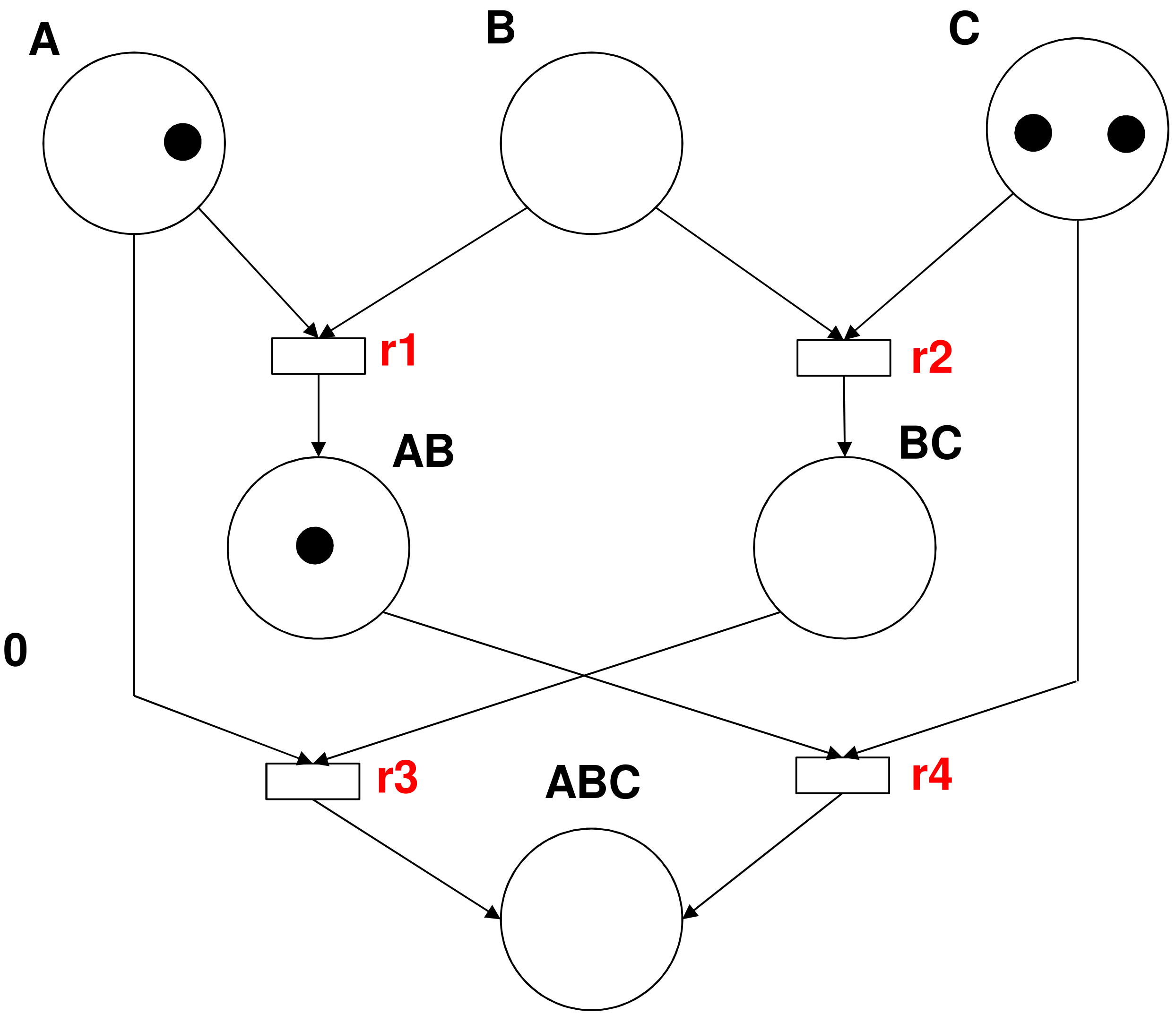
An example of transition system

$q_0(A) = 2$
$q_0(B) = 1$
$q_0(C) = 2$
$q_0(AB) = 0$
$q_0(BC) = 0$
$q_0(ABC) = 0$



An example of transition system

$q_1(A) = 1$
$q_1(B) = 0$
$q_1(C) = 2$
$q_1(AB) = 1$
$q_1(BC) = 0$
$q_1(ABC) = 0$



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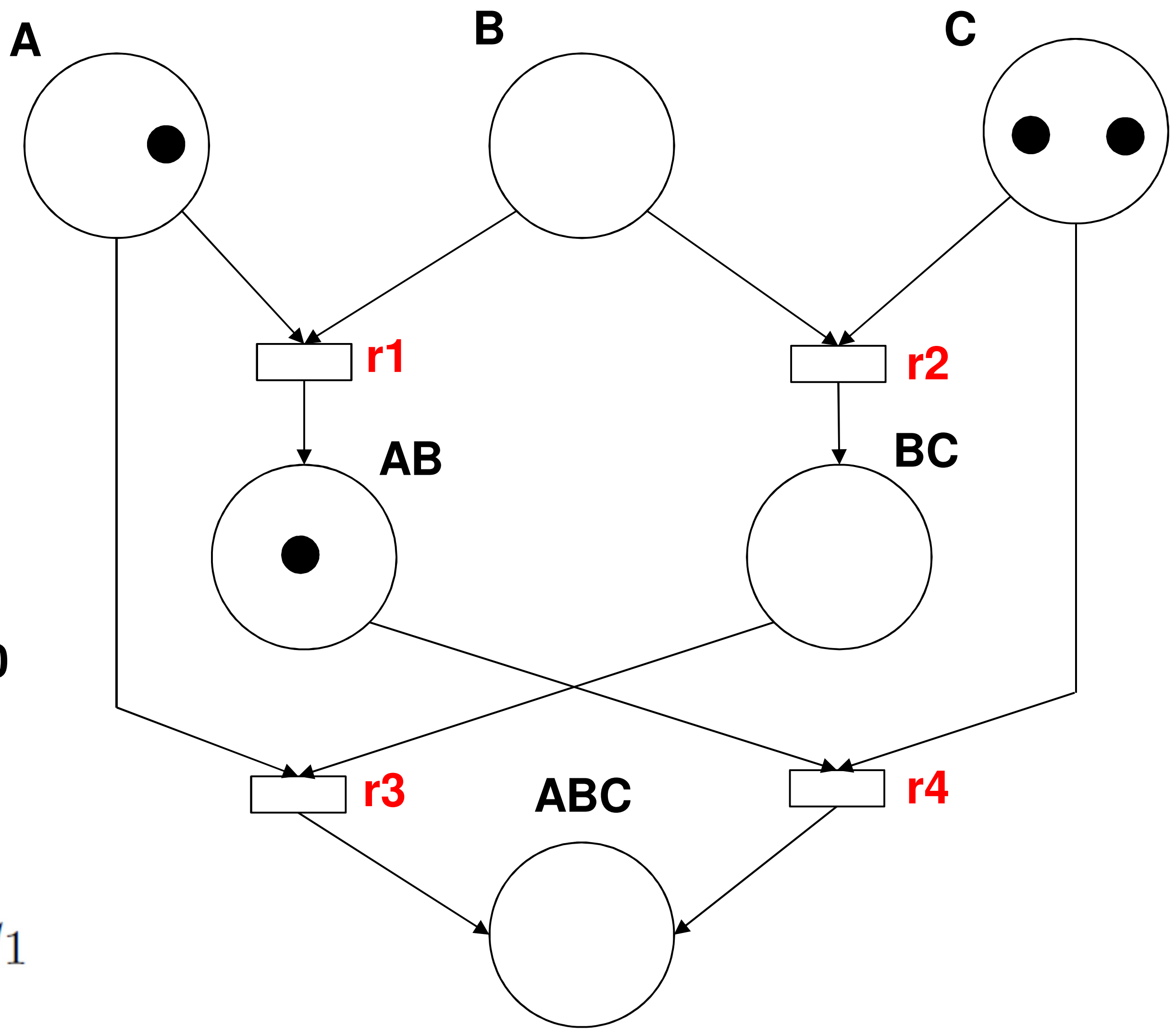
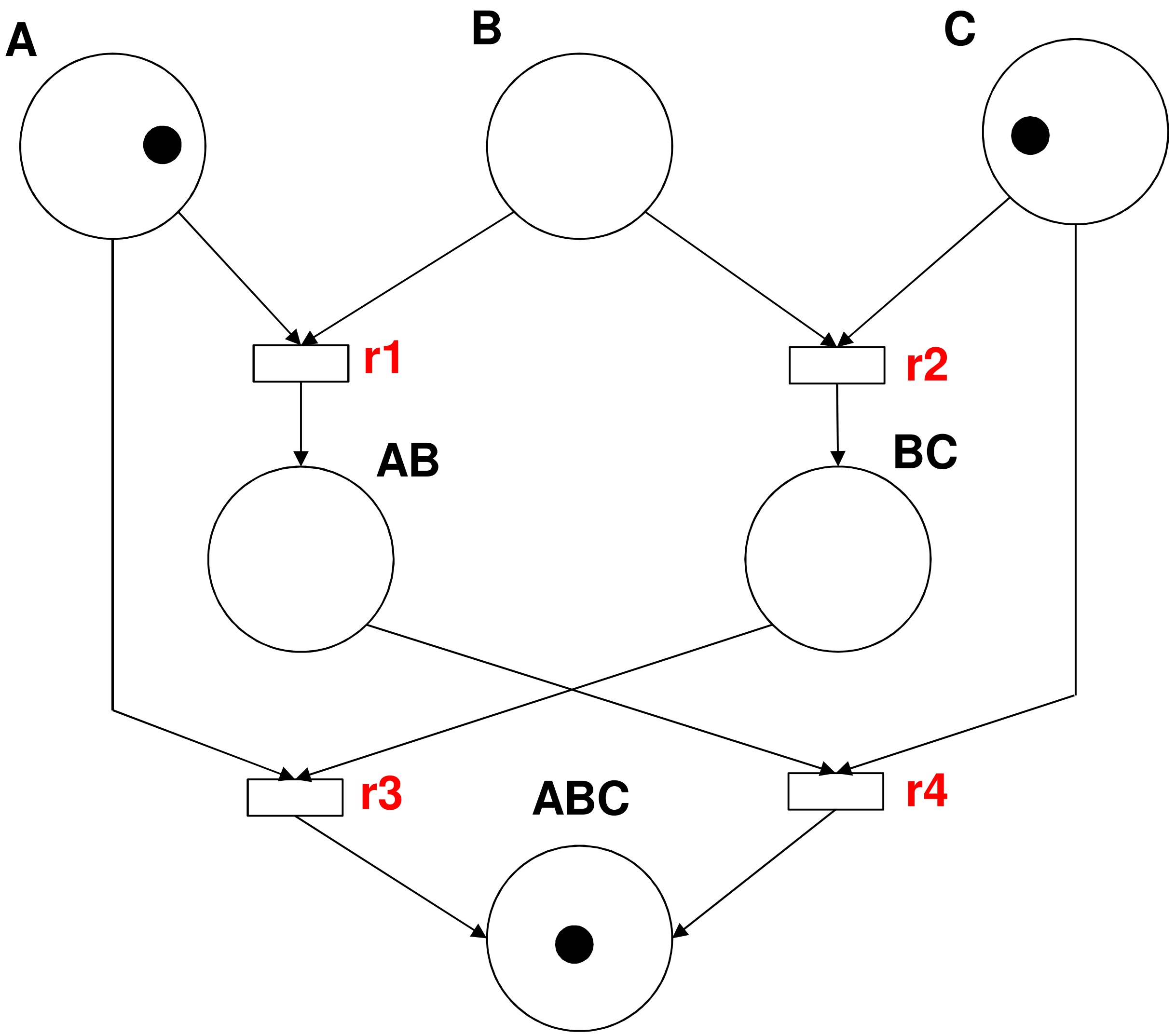


$q_1(A) = 1$
$q_1(B) = 0$
$q_1(C) = 2$
$q_1(AB) = 1$
$q_1(BC) = 0$
$q_1(ABC) = 0$

$$q_0 \xrightarrow{r_1} q_1$$

An example of transition system

$q_2(A) = 1$
$q_2(B) = 0$
$q_2(C) = 1$
$q_2(AB) = 0$
$q_2(BC) = 0$
$q_2(ABC) = 1$



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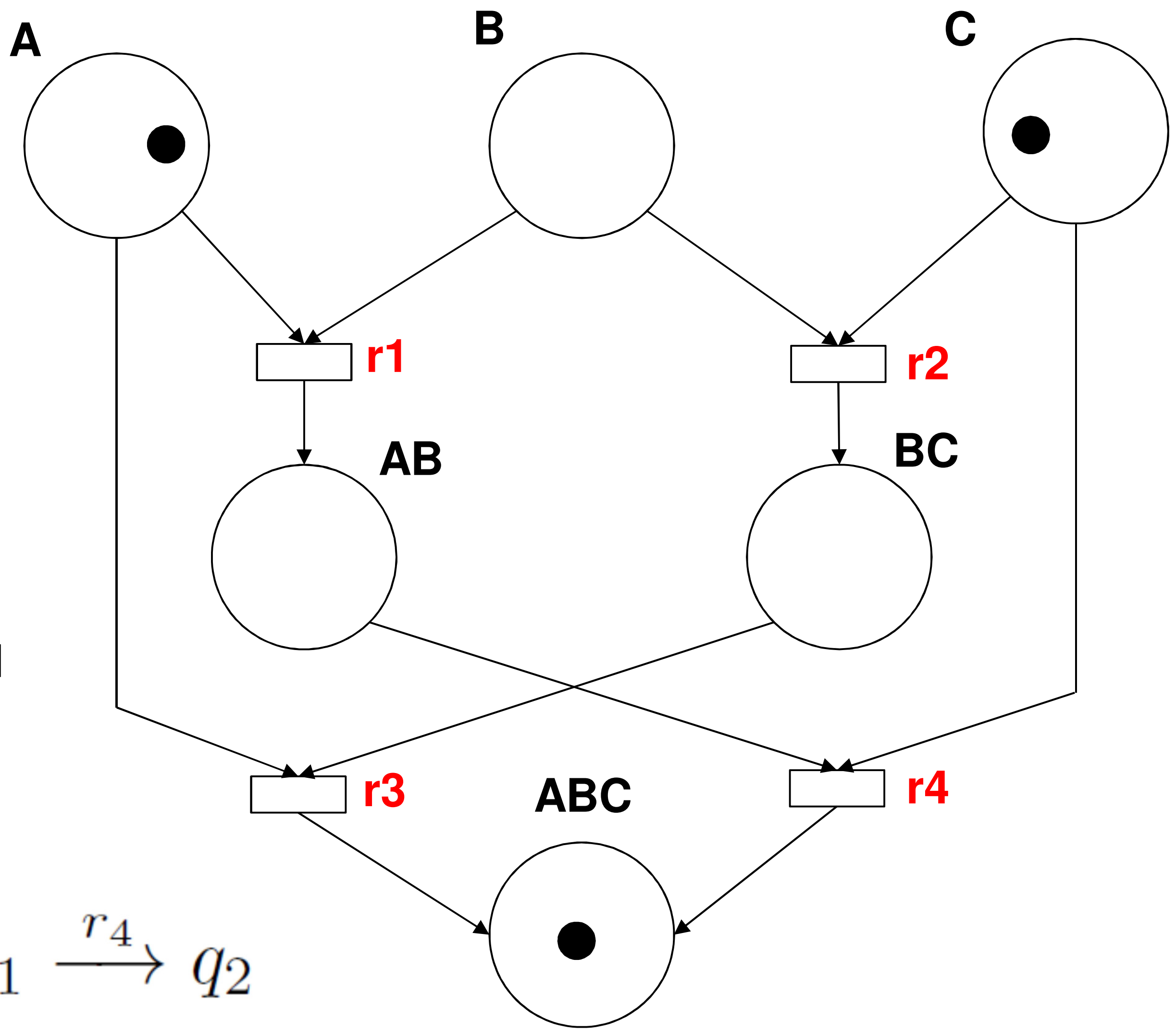


q2(A) = 1
q2(B) = 0
q2(C) = 1
q2(AB) = 0
q2(BC) = 0
q2(ABC) = 1

$$q_0 \xrightarrow{r_1} q_1 \xrightarrow{r_4} q_2$$

Derivation of a coarse-grained qualitative semantics

- Derivation of the abstract semantics using abstract interpretation framework

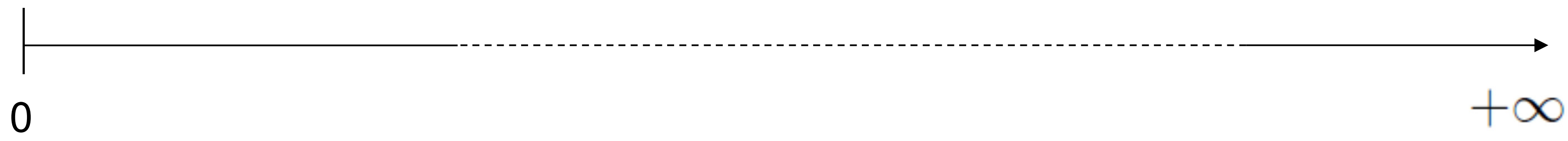
- Abstraction of values: quotienting of the domain of values by intervals

- Abstraction of traces: suppression of the ‘silent’ transitions

Derivation of a coarse-grained qualitative semantics

- **Abstraction of values:**

$\mathbb{R}^+$



Derivation of a coarse-grained qualitative semantics

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Derivation of a coarse-grained qualitative semantics

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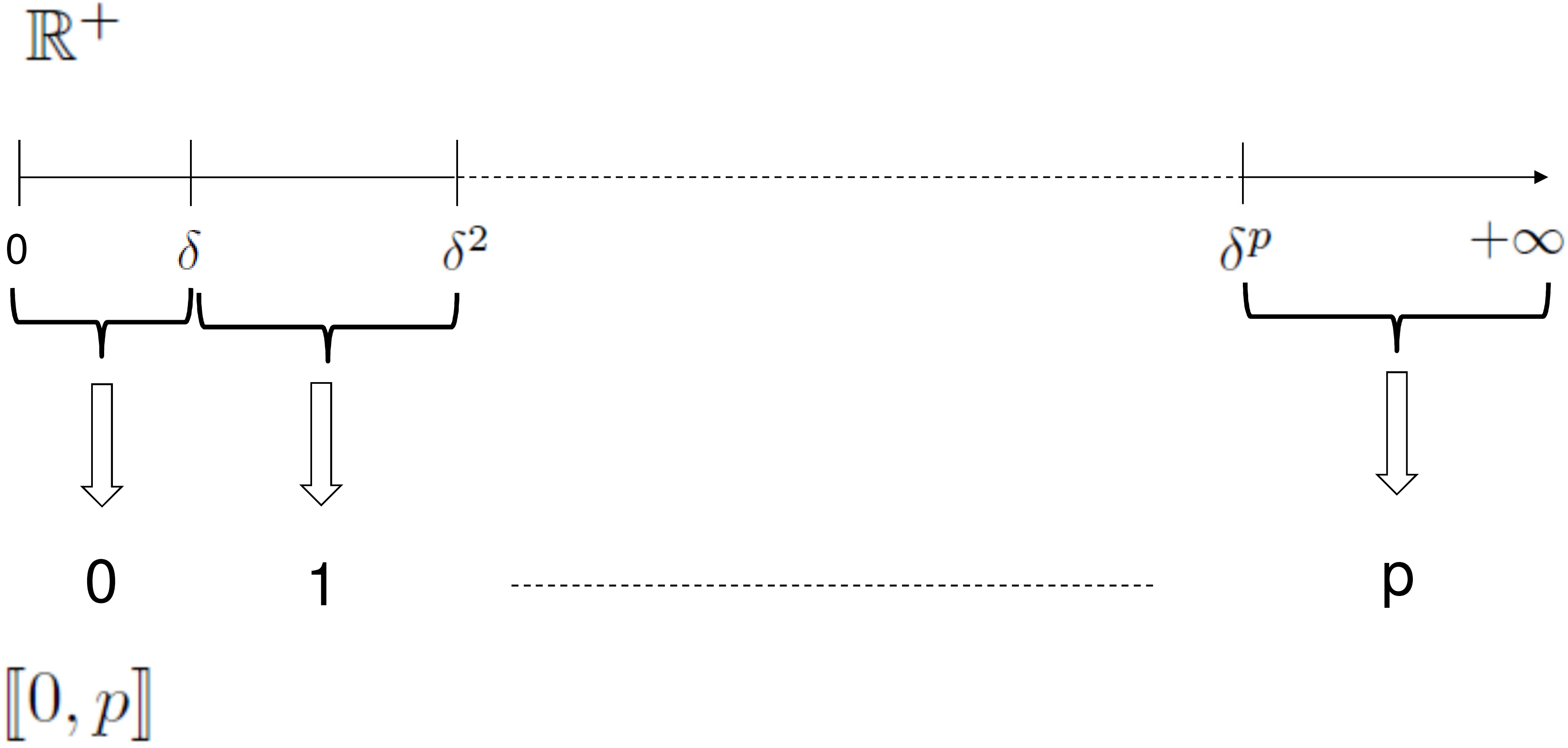

Derivation of a coarse-grained qualitative semantics

- **Abstraction of values:**

$$\beta^v : \begin{cases} \mathbb{R}^+ \longrightarrow [\![0, p]\!] \\ \quad t \longrightarrow \begin{cases} 0 \text{ if } t \in [0, \delta[\\ k \text{ if } t \in [\delta^k, \delta^{k+1}[\text{ for } k \in [\![1, p-1]\!] \\ p \text{ if } t \in [\delta^p, +\infty[\end{cases} \end{cases}$$

Derivation of a coarse-grained qualitative semantics

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- **Abstract transition system**

A reaction network R induces an abstract transition system $(\mathcal{Q}^\sharp_R, T^\sharp_R)$ where:
(1) $\mathcal{Q}^\sharp_R$, is the set $[\![0, p]\!]^\nu$;
(2) $T^\sharp_R$, is the subset of $[\![0, p]\!]^\nu \times [\![1, n]\!] \times [\![0, p]\!]^\nu$ defined by:

$$(q^\sharp, r, q'^\sharp) \in T^\sharp_R \Leftrightarrow \exists (q, r, q') \in T_R \text{ s.t. } q^\sharp = \beta^v \circ q \text{ and } q'^\sharp = \beta^v \circ q'.$$

Derivation of a coarse-grained qualitative semantics

- **Abstraction of prétraces**

Derivation of a coarse-grained qualitative semantics

- **Abstraction of prétraces**

$$(q_0',\ q_1 \xrightarrow{r_1} q_1',\ q_2 \xrightarrow{r_2} q_2')$$

Derivation of a coarse-grained qualitative semantics

- **Abstraction of prétraces**

$$(q'_0,\ q_1 \xrightarrow{r_1} q'_1,\ q_2 \xrightarrow{r_2} q'_2)$$

$$\Big\Downarrow\ \beta^t_1$$

$$(\beta^s(q'_0),\ \beta^s(q_1) \xrightarrow{r_1} \beta^s(q'_1),\ \beta^s(q_2) \xrightarrow{r_2} \beta^s(q'_2))$$

Derivation of a coarse-grained qualitative semantics

- **Abstraction of prétraces**

$$(q_0'^{\sharp},\ q_1^{\sharp} \overset{r_1}{\rightsquigarrow} q_1^{\sharp},\ q_2^{\sharp} \overset{r_2}{\rightsquigarrow} q_2'^{\sharp})$$

Derivation of a coarse-grained qualitative semantics

- **Abstraction of prétraces**

$$\left(q_0'^{\sharp},\ q_1^{\sharp} \overset{r_1}{\rightsquigarrow} q_1^{\sharp},\ q_2^{\sharp} \overset{r_2}{\rightsquigarrow} q_2'^{\sharp}\right)$$

$$\Big\Downarrow\ \beta_2^t$$

$$\left(q_0'^{\sharp},\ q_2^{\sharp} \overset{r_2}{\rightsquigarrow} q_2'^{\sharp}\right)$$

Derivation of a coarse-grained qualitative semantics

- **Abstraction of prétraces**

$$\beta^t = \beta_2^t \circ \beta_1^t$$

$$\beta_1^t : \begin{cases} \mathcal{Q}_R \times T_R^\star \longrightarrow \mathcal{Q}_R \times T_R^\star \\ (q'_0, (q_i, r_i, q'_i)_{1\leq i\leq k}) \longmapsto (\beta^s(q'_0), (\beta^s(q_i), r_i, \beta^s(q'_i)))_{1\leq i\leq k} \end{cases}$$

$$\beta_2^t : \begin{cases} \mathcal{Q}_R^\sharp \times T_R^{\sharp\star} \longrightarrow \mathcal{Q}_R^\sharp \times T_{R/\varepsilon}^{\sharp\star} \\ ({q_0^\sharp}', (q_i^\sharp, r_i, {q_i^\sharp}')) \longmapsto ({q_0^\sharp}', (q_{\sigma(i)}^\sharp, r_i, {q^\sharp}'_{\sigma(i)})) \end{cases}$$

where $\sigma(i)$ ranges over the set $\{i \in [\![1,k]\!] \mid q_i^\sharp \neq {q_i^\sharp}'\}$ in increasing order.

Derivation of a coarse-grained qualitative semantics

- **Abstraction of prétraces**

$$\mathbb{F}^{\sharp}_{\mathcal{Q}_{R,0}} : \begin{cases} \wp(\mathcal{Q}^{\sharp}_{R} \times T^{\sharp\star}_{R/\varepsilon}) \longrightarrow \wp(\mathcal{Q}^{\sharp}_{R} \times T^{\sharp\star}_{R/\varepsilon}) \\ \qquad\qquad X \longmapsto \{(\alpha^{t} \circ \mathbb{F}_{\mathcal{Q}_{R,0}} \circ \gamma^{t})(t) \mid t \in X\} \end{cases}$$

where:

$$\alpha^{t} : \begin{cases} \wp(\mathcal{Q}_{R} \times T^{\star}_{R}) \longrightarrow \wp(\mathcal{Q}^{\sharp}_{R} \times T^{\sharp\star}_{R/\varepsilon}) \\ \qquad\qquad X \longmapsto \{\beta^{t}(x) \in \mathcal{Q}^{\sharp}_{R} \times T^{\sharp\star}_{R/\varepsilon} \mid x \in X\} \end{cases}$$

$$\gamma^{t} : \begin{cases} \wp(\mathcal{Q}^{\sharp}_{R} \times T^{\sharp\star}_{R/\varepsilon}) \longrightarrow \wp(\mathcal{Q}_{R} \times T^{\star}_{R}) \\ \qquad\qquad Y \longmapsto \{x \in \mathcal{Q}_{R} \times T^{\star}_{R} \mid \beta^{t}(x) \in Y\} \end{cases}$$

Derivation of a coarse-grained qualitative semantics

- **Abstraction of prétraces**

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(α^{t}, γ^{t}) is a Galois connection.

Derivation of a coarse-grained qualitative semantics

- **Abstract trace semantics**

$$\mathcal{T}^{\sharp}_{\mathcal{Q}_{R,0}} = \mathit{lfp}\ \mathbb{F}^{\sharp}_{\mathcal{Q}_{R,0}}$$

- **Theorem of fixpoint transfert**

For any reaction network R and any set of initial states $\mathcal{Q}_{R,0} \subseteq \mathcal{Q}_R$:

$$\mathit{lfp}\ \mathbb{F}_{\mathcal{Q}_{R,0}} \subseteq \gamma^t(\mathit{lfp}\ \mathbb{F}^{\sharp}_{\mathcal{Q}_{R,0}}).$$

Derivation of a coarse-grained qualitative semantics

- **Property**

(1) For any abstract transition $(q^\sharp, r, q^{\sharp\prime}) \in T_R^\sharp$, if $\delta > V_\infty$, then:
- $q^{\sharp\prime}(x) = q^\sharp(x)$ or
- $q^{\sharp\prime}(x) = q^\sharp(x) + sign(V_r(x))$.

(2) For any rule r and any abstract state $q^\sharp \in Q_R^\sharp$, if $\delta > M_\infty$, then, for any chemical species $y \in \nu$ s.t. $V_r(y) \neq 0$ and $0 \leq q^\sharp(y) + sign(V_r(y)) \leq p$:

$$q^\sharp, r, q^\sharp[y \mapsto q^\sharp(y) + sign(V_r(y))]) \in T_R^\sharp.$$

Derivation of a coarse-grained qualitative semantics

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$$q^\sharp, r, q^\sharp[y \mapsto q^\sharp(y) + sign(V_r(y))]) \in T_R^\sharp.$$

$\Longrightarrow$ Too coarse abstraction!

Application to the case study showing a race between unary and binary reactions

- Reaction scheme

$$\begin{cases} 2A \xrightarrow{k_1} B \\ A \xrightarrow{k_2} C \end{cases}$$

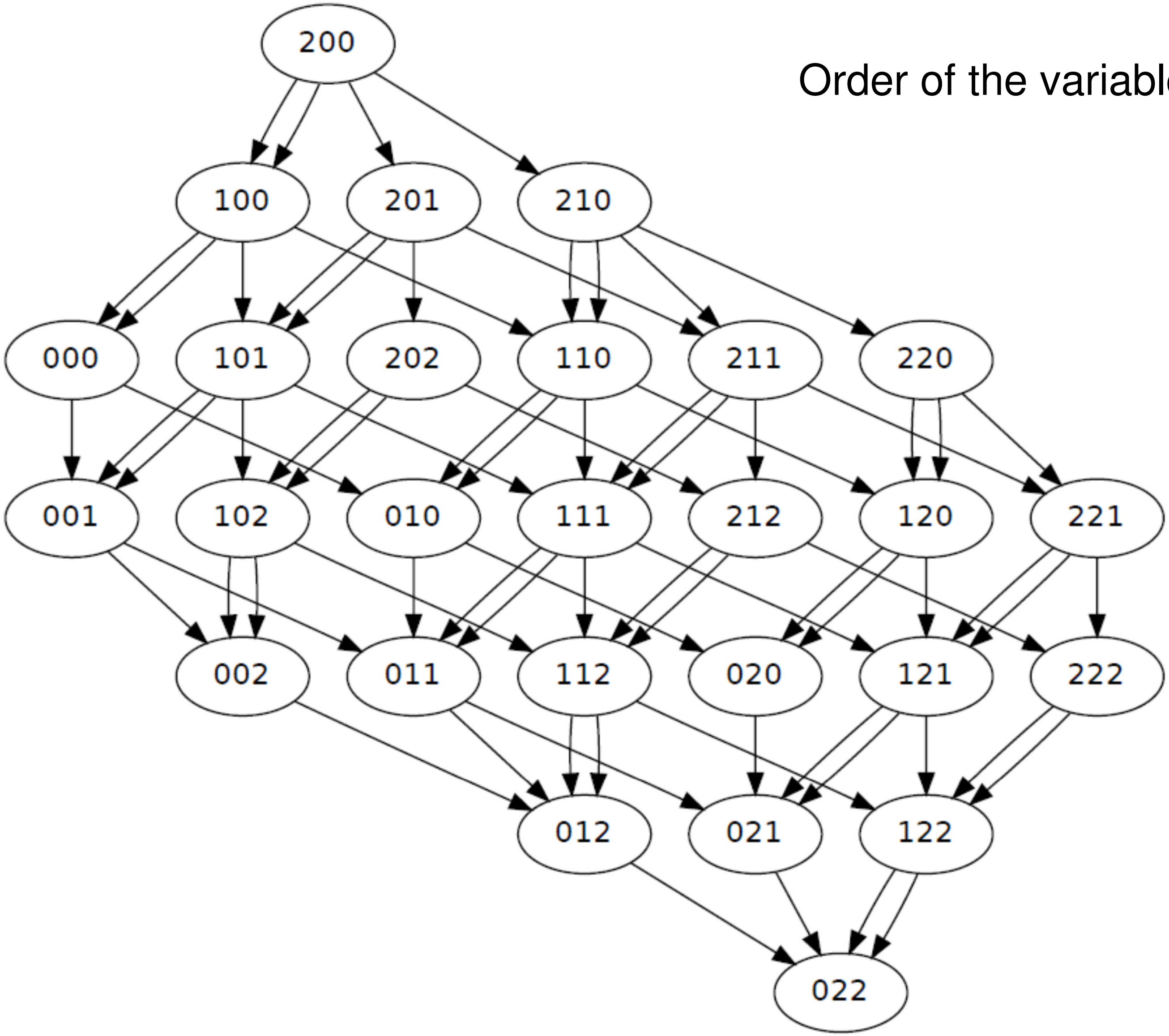
- Properties

$$k_2 \cdot A_{in} \ll k_1 \Longrightarrow C_{eq} \gg B_{eq}$$

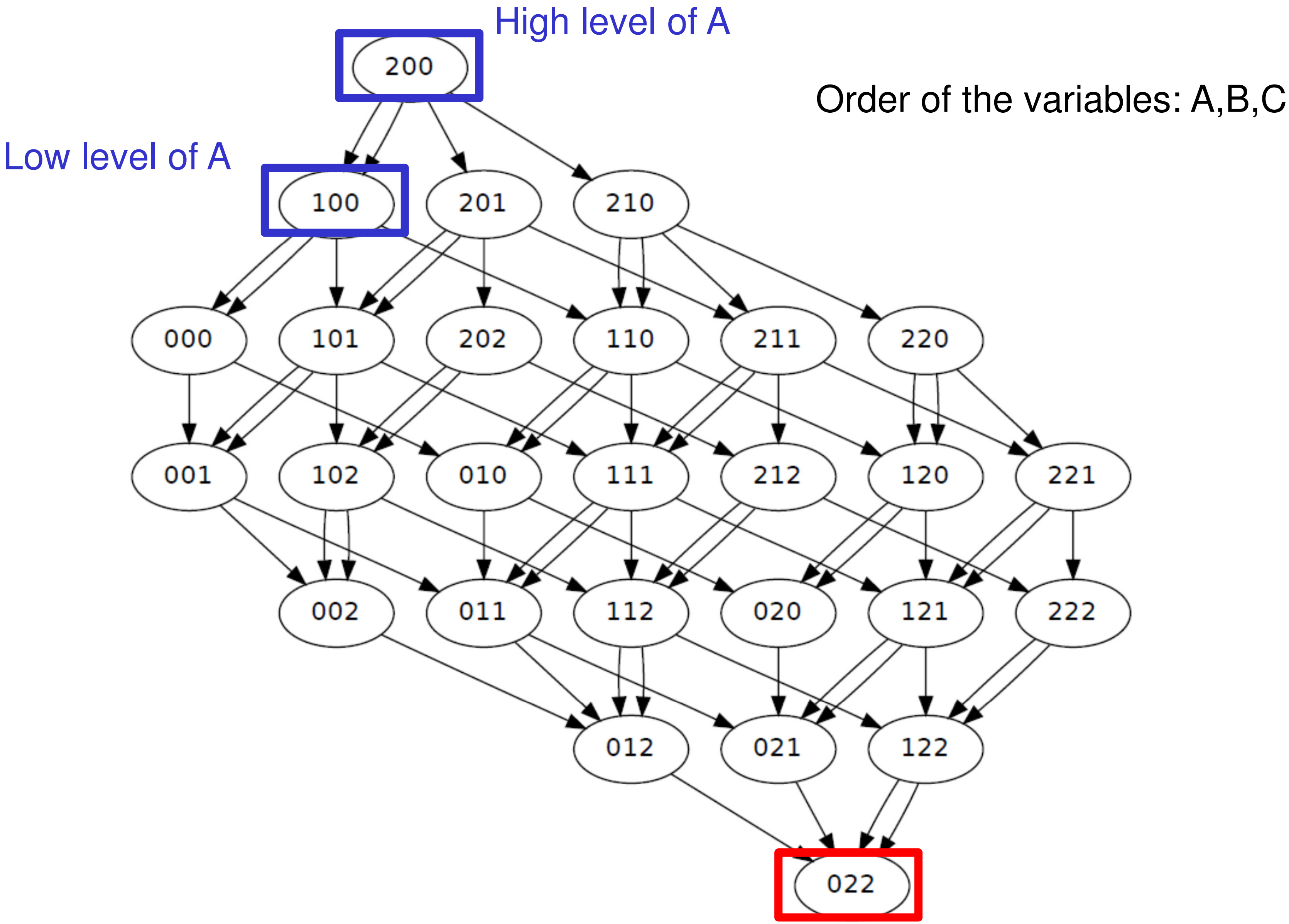
$$k_2 \cdot A_{in} \gg k_1 \Longrightarrow C_{eq} \ll B_{eq}$$

Application to the case study showing a race between unary and binary reactions

Order of the variables: A,B,C



Application to the case study showing a race between unary and binary reactions



Refinements of the abstract semantics

Introduction of three refinements

- Mass invariants

- Limiting resources for the crossing of intervals

- Incorporation of kinetic information

Mass invariants

- An example of mass invariant in our case study

$$
\begin{cases}
A + B \overset{k_1}{\rightarrow} AB \\
B + C \overset{k_2}{\rightarrow} BC \\
A + BC \overset{k_1}{\rightarrow} ABC \\
AB + C \overset{k_2}{\rightarrow} ABC
\end{cases}
$$

$$
\begin{aligned}
q(A) + q(AB) + q(ABC) &= A_T \\
q(B) + q(AB) + q(BC) + q(ABC) &= B_T \\
q(C) + q(BC) + q(ABC) &= C_T
\end{aligned}
$$

Mass invariants

- Trace invariant

$$inv \subseteq \mathcal{Q}_R \times T_R^\star \text{ s.t. } \mathbb{F}_{\mathcal{Q}_{R,0}}(inv) \subseteq inv$$

- Theorem (abstract trace semantics with invariants)

Let $\mathcal{Q}'_{R,0} \subseteq \mathcal{Q}_{R,0}$ *and* $inv \subseteq \mathcal{T}_{R,\mathcal{Q}_{R,0}}$ *s.t.* $\mathbb{F}_{\mathcal{Q}'_{R,0}}(inv) \subseteq inv$. *Then:*

$$\mathcal{T}_{R,\mathcal{Q}'_{R,0}} \subseteq \gamma^t(\mathit{lfp}\,[Y \mapsto \mathbb{F}^\sharp_{\mathcal{Q}'_{R,0}}(Y) \cap \alpha^t(inv)]).$$

Mass invariants

- Property (computation of the invariant in the abstract)

$(a_x)_{x\in\nu} \in \mathbb{N}^{\nu} \setminus \{0\}^{\nu}$
$b \in \mathbb{N}$
$q^{\sharp} \in \mathcal{Q}_R^{\sharp}$
$S = \sum_{x\in\nu} a_x$
$q^{\sharp}_{max} = max\{k \in [\![0, p]\!] \mid \exists x \in \nu,\ a_x > 0 \ \wedge\ k = q^{\sharp}(x)\}.$

We assume that $S < \delta$. Then, if either $S\delta^{\beta^{v}(b)} \leq b$ or $\beta^{v}(b) = 0$:

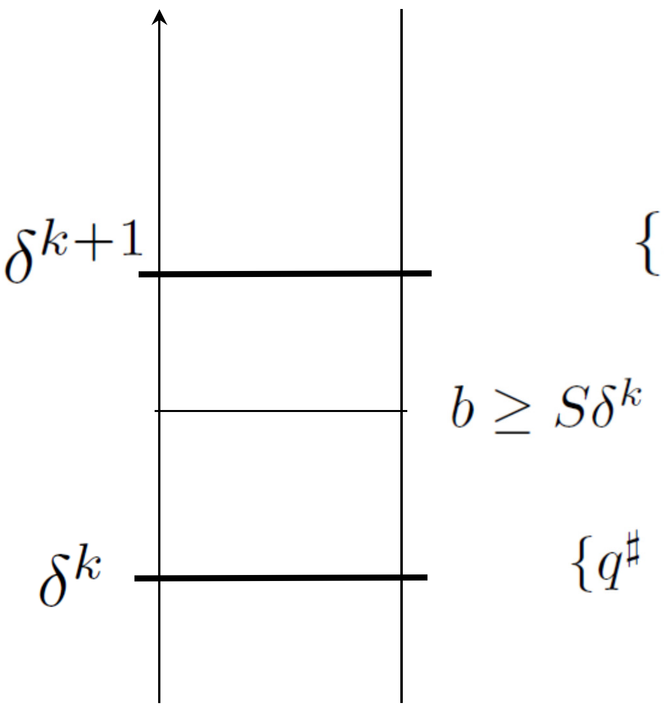
$$\alpha^{s}(\{q \in \mathcal{Q}_R \mid b = \textstyle\sum_{x\in\nu} \alpha_x q(x)\}) = \{q^{\sharp} \in \mathcal{Q}_R^{\sharp} \mid q^{\sharp}_{max} = \beta^{v}(b)\}$$

Otherwise:

$$\alpha^{s}(\{q \in \mathcal{Q}_R \mid b = \textstyle\sum_{x\in\nu} \alpha_x q(x)\}) = \{q^{\sharp} \in \mathcal{Q}_R^{\sharp} \mid q^{\sharp}_{max} \in \{\beta^{v}(b) - 1, \beta^{v}(b)\}\}.$$

Mass invariants

- An example



$$\{q \mid q(A) + \ q(AB) + \ q(ABC) = b\}$$

$$\Big\Downarrow \alpha^s$$

$$\{q^\sharp \mid max(q^\sharp(A),\ q^\sharp(AB),\ q^\sharp(ABC)) = \beta^v(b)\}$$

Limiting resources for interval crossing

- An example in our case study

$$\begin{cases} A + B \overset{k_1}{\rightarrow} AB \\ B + C \overset{k_2}{\rightarrow} BC \\ A + BC \overset{k_1}{\rightarrow} ABC \\ AB + C \overset{k_2}{\rightarrow} ABC \end{cases}$$

$$\beta^s(q)(A) = 0$$
$$\beta^s(q)(C) = 0$$
$$\beta^s(q)(ABC) = 0$$

Limiting resources for interval crossing

- An example in our case study

$$\begin{cases} A + B \xrightarrow{k_1} AB \\ B + C \xrightarrow{k_2} BC \\ A + BC \xrightarrow{k_1} ABC \\ AB + C \xrightarrow{k_2} ABC \end{cases}$$

$$\begin{aligned} \beta^s(q)(A) &= 0 \\ \beta^s(q)(C) &= 0 \\ \beta^s(q)(ABC) &= 0 \end{aligned} \quad \Longrightarrow \quad \begin{aligned} \beta^s(q)(A) &= 0 \\ \beta^s(q)(C) &= 0 \\ \beta^s(q)(ABC) &= 1 \end{aligned}$$

Limiting resources for interval crossing

- An example in our case study

$$\begin{cases} A + B \overset{k_1}{\rightarrow} AB \\ B + C \overset{k_2}{\rightarrow} BC \\ A + BC \overset{k_1}{\rightarrow} ABC \\ AB + C \overset{k_2}{\rightarrow} ABC \end{cases}$$

$$\begin{array}{l} \beta^s(q)(A) = 0 \\ \beta^s(q)(C) = 0 \\ \beta^s(q)(ABC) = 0 \end{array} \quad \longrightarrow \quad \begin{array}{l} \beta^s(q)(A) = 0 \\ \beta^s(q)(C) = 0 \\ \beta^s(q)(ABC) = 1 \end{array} \quad \cancel{\xrightarrow{*}} \quad \beta^s(q)(ABC) = 2$$

Scale separation

- Reactions can occur at different time scales

- Need to account for this information in order to capture the properties of interest of our case study

$$
\begin{cases}
A + B \xrightarrow{k_1} AB \\
B + C \xrightarrow{k_2} BC \\
A + BC \xrightarrow{k_1} ABC \\
AB + C \xrightarrow{k_2} ABC
\end{cases}
$$

Scale separation

- Reactions can occur at different time scales

- Need to account for this information in order to capture the properties of interest of our case study

$$\begin{cases} A + B \overset{k_1}{\rightarrow} AB \\ B + C \overset{k_2}{\rightarrow} BC \\ A + BC \overset{k_1}{\rightarrow} ABC \\ AB + C \overset{k_2}{\rightarrow} ABC \end{cases}$$

Cannot capture the sequestration effect if we do not neglect the reaction

A + BC -> ABC   when B >> 1 and BC << 1

Scale separation

- Assignement of a kinetic function to each reaction

$$k_r(q) \subseteq \wp(\mathbb{R}^+) \setminus \{\emptyset\}$$

- Separation of time scales encoded by a subset $Sep \subseteq (\mathbb{R}^+)^2$

- Refinement of the concrete transitions

$(q, r, q') \in T^{\mathrm{TIME}}_{R,Sep}$ s.t. for each $(r, q'') \in [\![1, n]\!] \times \mathcal{Q}_R$:

$$(q, r', q'') \in T_R \Rightarrow (max(k_r(q)), min(k_{r'}(q))) \notin Sep$$

- Parameter $slow^\sharp \subseteq \mathcal{Q}^\sharp_R \times [\![1, n]\!]$

For any pair $(q^\sharp, r) \in slow^\sharp$ and any concrete state q such that $\beta^s(q) = q^\sharp$, there exists a rule index r' s.t. $(max(k_r(q), min(k_{r'}(q)) \in Sep$.

Scale separation

- Refinement of the abstract semantics

- Theorem of soundness

- Property (computation of the parameter $slow^\sharp$ in the abstract)

Application to our case studies

- **Modeling assumptions**

$$\delta > 5$$

$$\Rightarrow \quad \delta > M_\infty$$

$$\Rightarrow \quad \delta > 2V_\infty$$

$$\Rightarrow \quad \delta > S$$

where S is the sum of the coefficients of the semi-positive constraints used as a mass preservation invariant

Application to our case studies

- **Modeling assumptions**

Mass action stochastic law for the definition of the kinetic function

$$k_r(q) = a_r \times \prod_{x \in \nu} \left(\frac{q(x)!}{(q(x) - M_r(x))!\, M_r(x)!} \;\middle|\; M_r(x) \neq 0 \right)$$

$$a_r = \delta^m \text{ with } 1 \leq m \leq p$$

Asynchronous updating policy

Application to the case study showing a sequestration effect

- Reaction scheme:

$$\begin{cases} A + B \overset{k_1}{\rightarrow} AB \\ B + C \overset{k_2}{\rightarrow} BC \\ A + BC \overset{k_1}{\rightarrow} ABC \\ AB + C \overset{k_2}{\rightarrow} ABC \end{cases}$$

- Sequestration property

$$B_T \gg max\{A_T, C_T\} \Rightarrow ABC_{eq} \ll 1$$

Application to the case study showing a sequestration effect

- Mass invariant

$$\begin{aligned} q(A) + q(AB) + q(ABC) &= A_T \\ q(B) + q(AB) + q(BC) + q(ABC) &= B_T \\ q(C) + q(BC) + q(ABC) &= C_T \end{aligned}$$

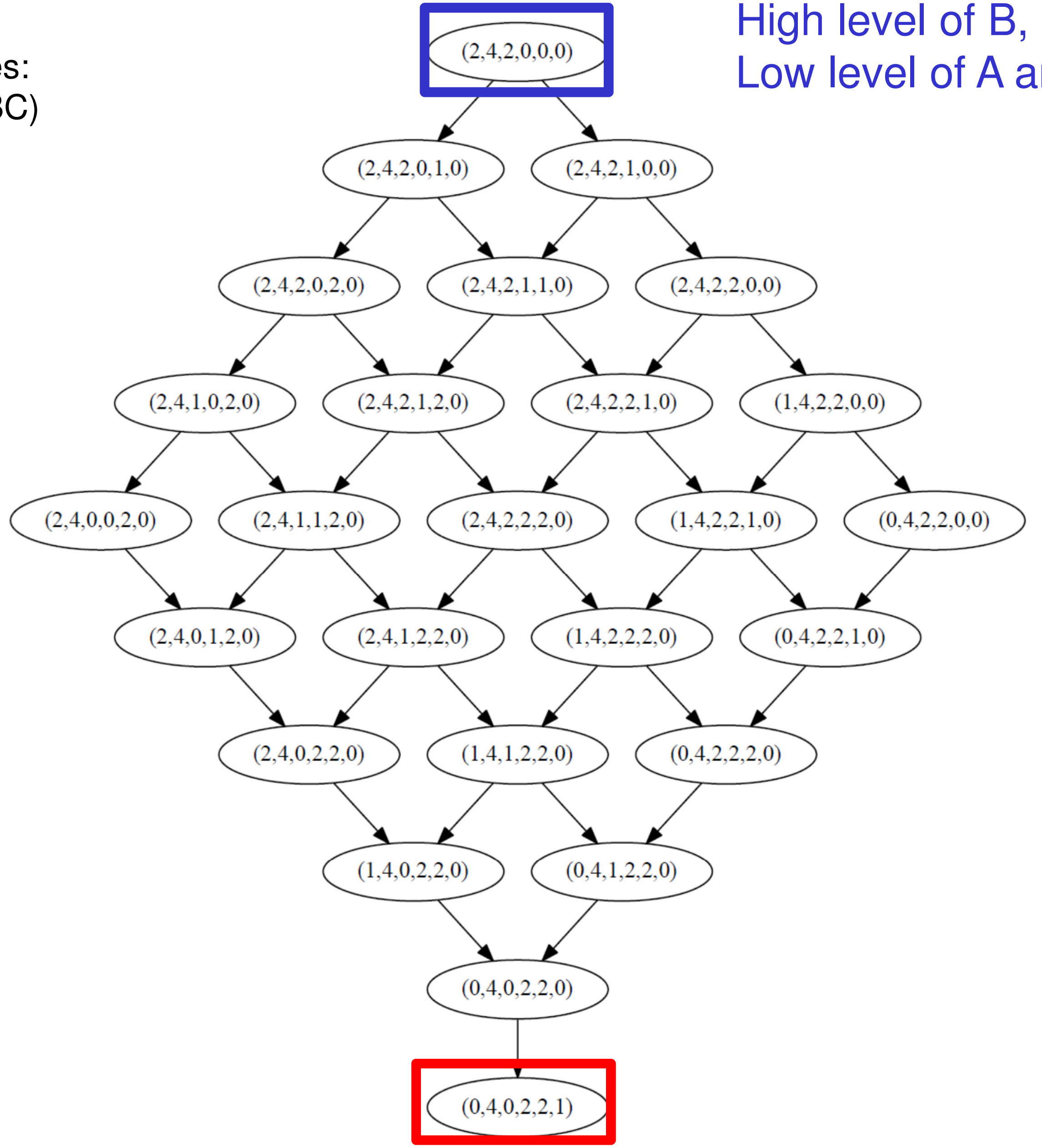
- Constantes cinétiques

$$a_{r1} = a_{r2} = a_{r3} = a_{r4} = 1$$

Application to the case study showing a sequestration effect

Order of the variables:
(A, B, C, AB, BC, ABC)

$$A_T = 3\delta^2$$
$$B_T = 4\delta^4$$
$$C_T = 3\delta^2$$



High level of B,
Low level of A and C

Application to the case study showing a sequestration effect

Order of the variables:
(A, B, C, AB, BC, ABC)

$$A_T = 3\delta^2$$
$$B_T = 4\delta^4$$
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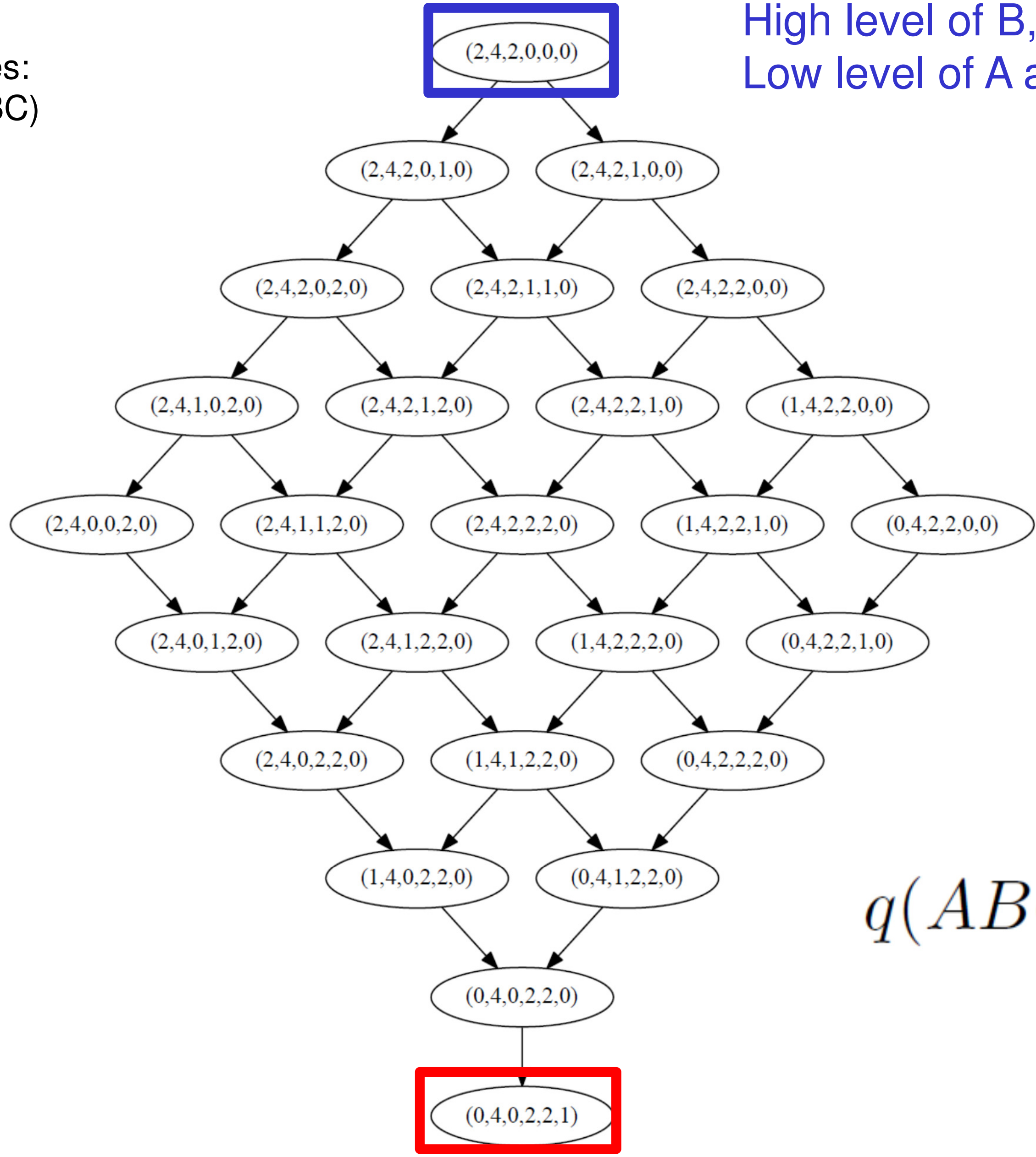


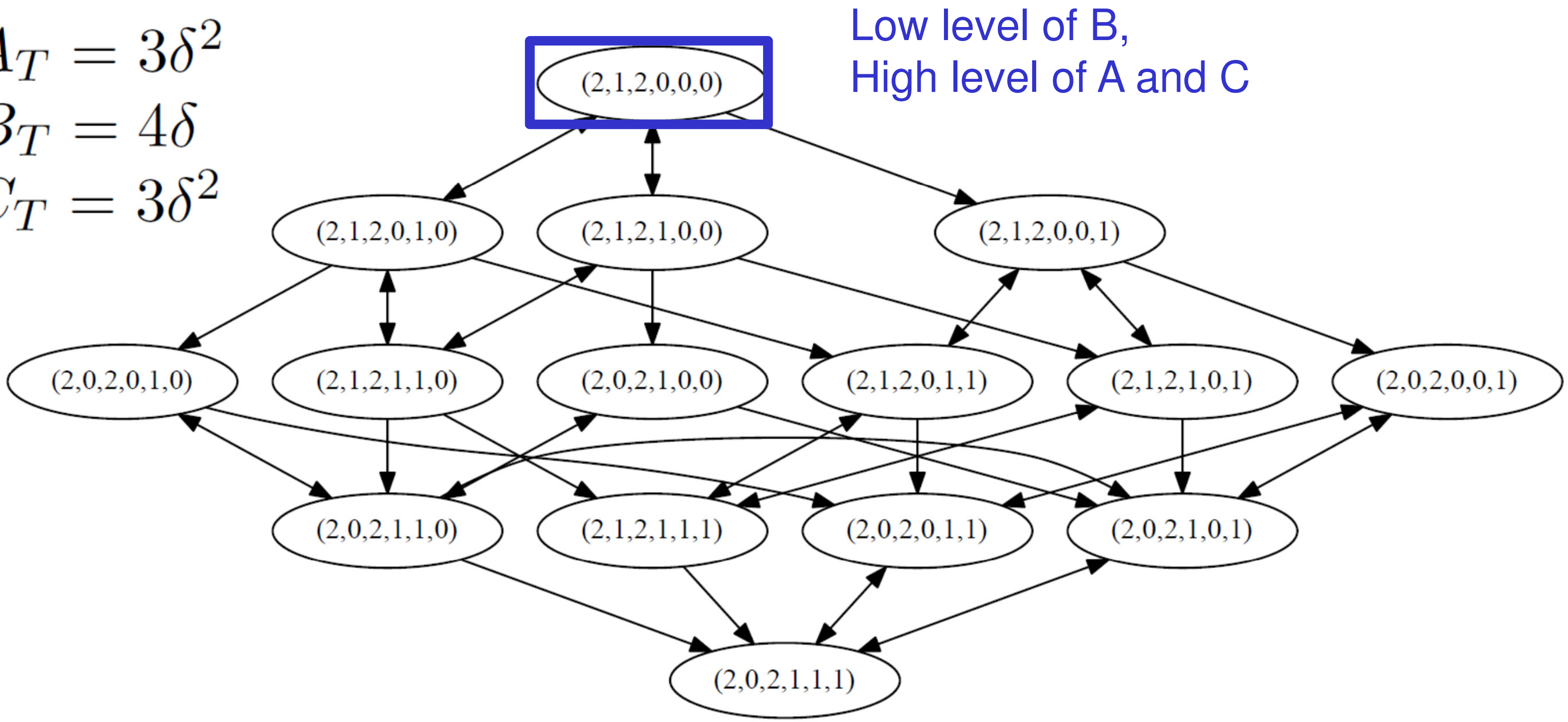
High level of B,
Low level of A and C

$$q(ABC) < \delta^2$$

Application to the case study showing a sequestration effect

Order of the variables:
(A, B, C, AB, BC, ABC)

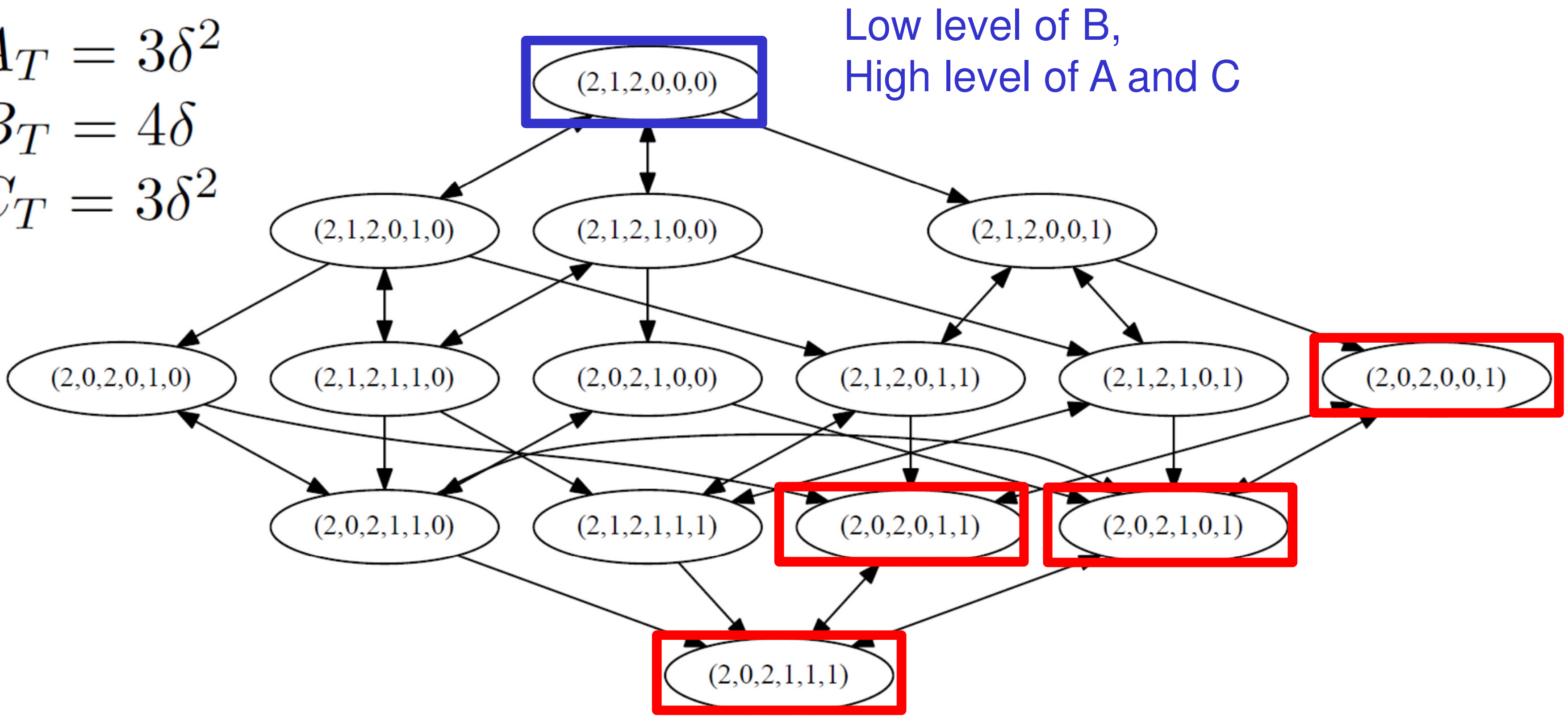
$$A_T = 3\delta^2$$
$$B_T = 4\delta$$
$$C_T = 3\delta^2$$



Application to the case study showing a sequestration effect

Order of the variables:
(A, B, C, AB, BC, ABC)

$$A_T = 3\delta^2$$
$$B_T = 4\delta$$
$$C_T = 3\delta^2$$



Application to the case study showing a race between unary and binary reactions

- Reaction scheme

$$\begin{cases} 2A \overset{k_1}{\rightarrow} B \\ A \overset{k_2}{\rightarrow} C \end{cases}$$

- Properties

$$k_2 \cdot A_{in} \ll k_1 \Longrightarrow C_{eq} \gg B_{eq}$$

$$k_2 \cdot A_{in} \gg k_1 \Longrightarrow C_{eq} \ll B_{eq}$$

Application to the case study showing a race between unary and binary reactions

- Mass invariant

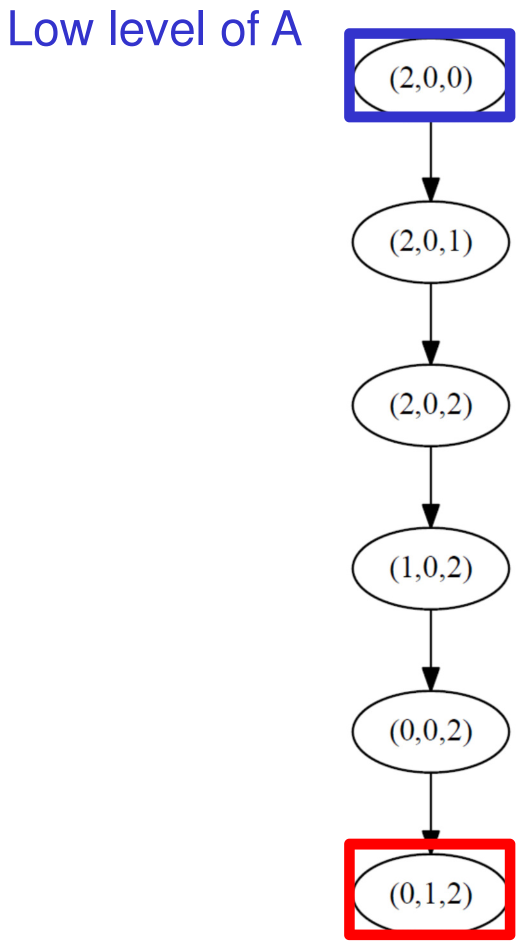
$$q(A) + 2q(B) + q(C) = A_T$$

- Constantes cinétiques

$$a_{r1} = 1 \quad a_{r2} = \delta^4$$

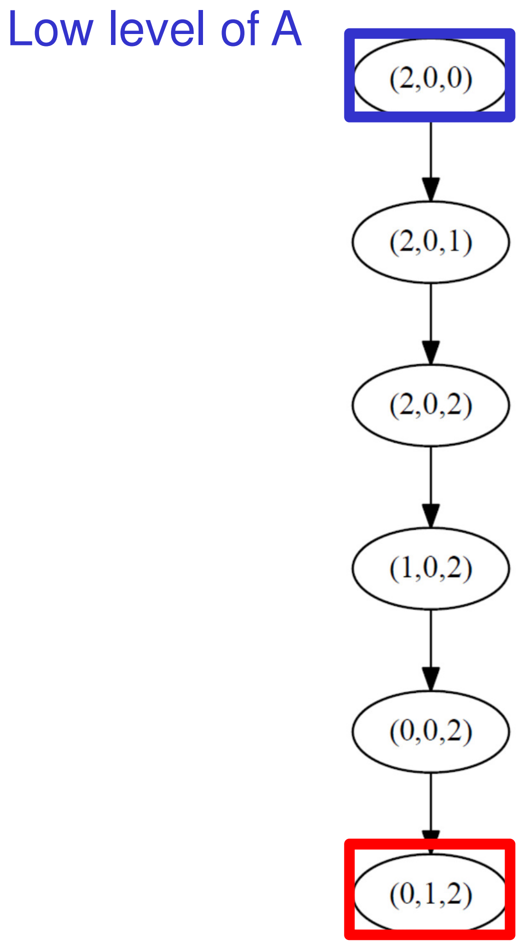
Application to the case study showing a race between unary and binary reactions

$$A_T = 4\delta^2$$



Application to the case study showing a race between unary and binary reactions

$$A_T = 4\delta^2$$

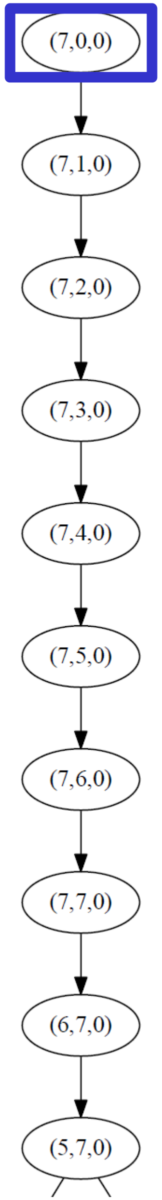


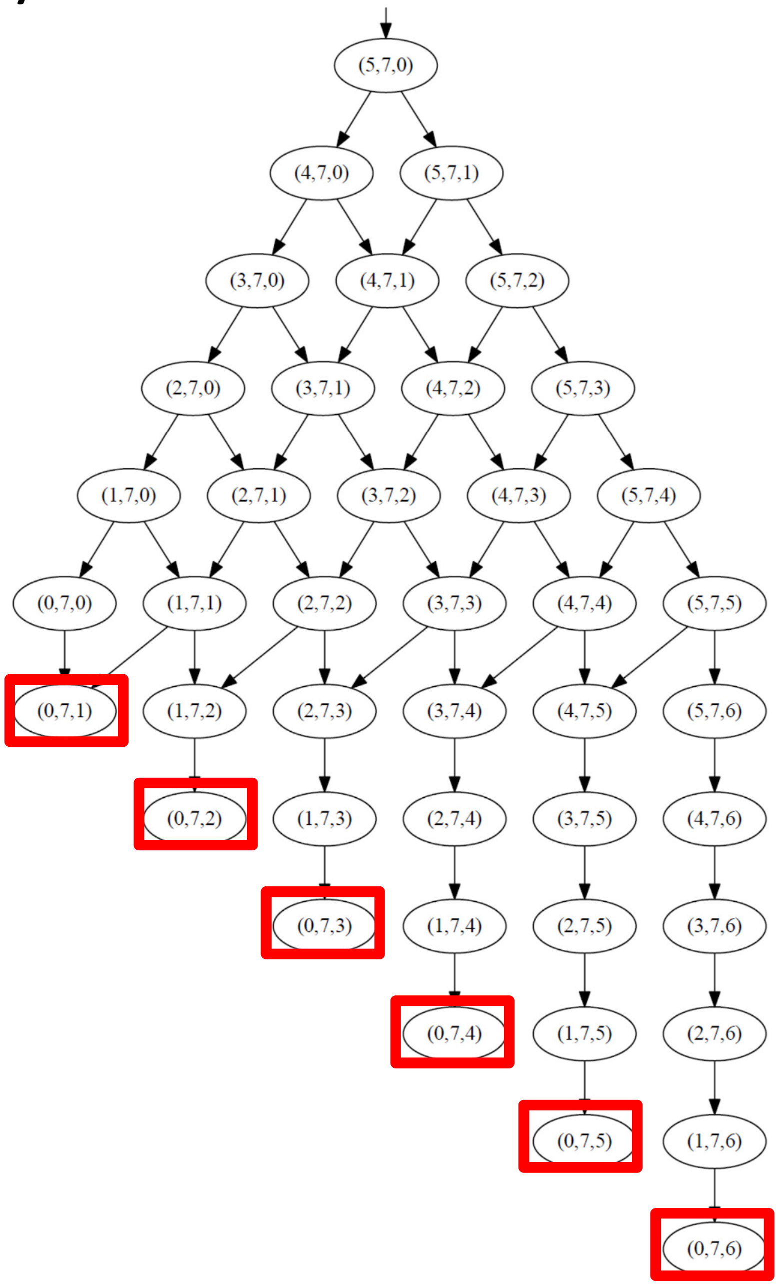
$$q(B) \leq q(C)$$

Application to the case study showing a race between unary and binary reactions

High level of A

$$A_T = 4\delta^7$$

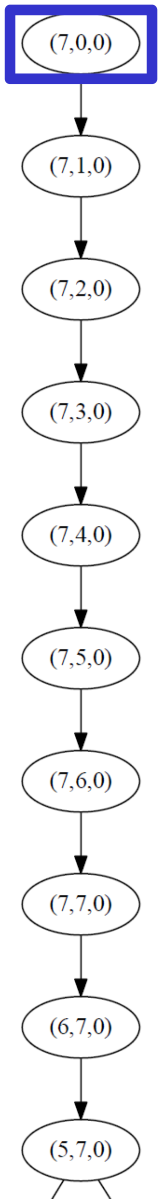




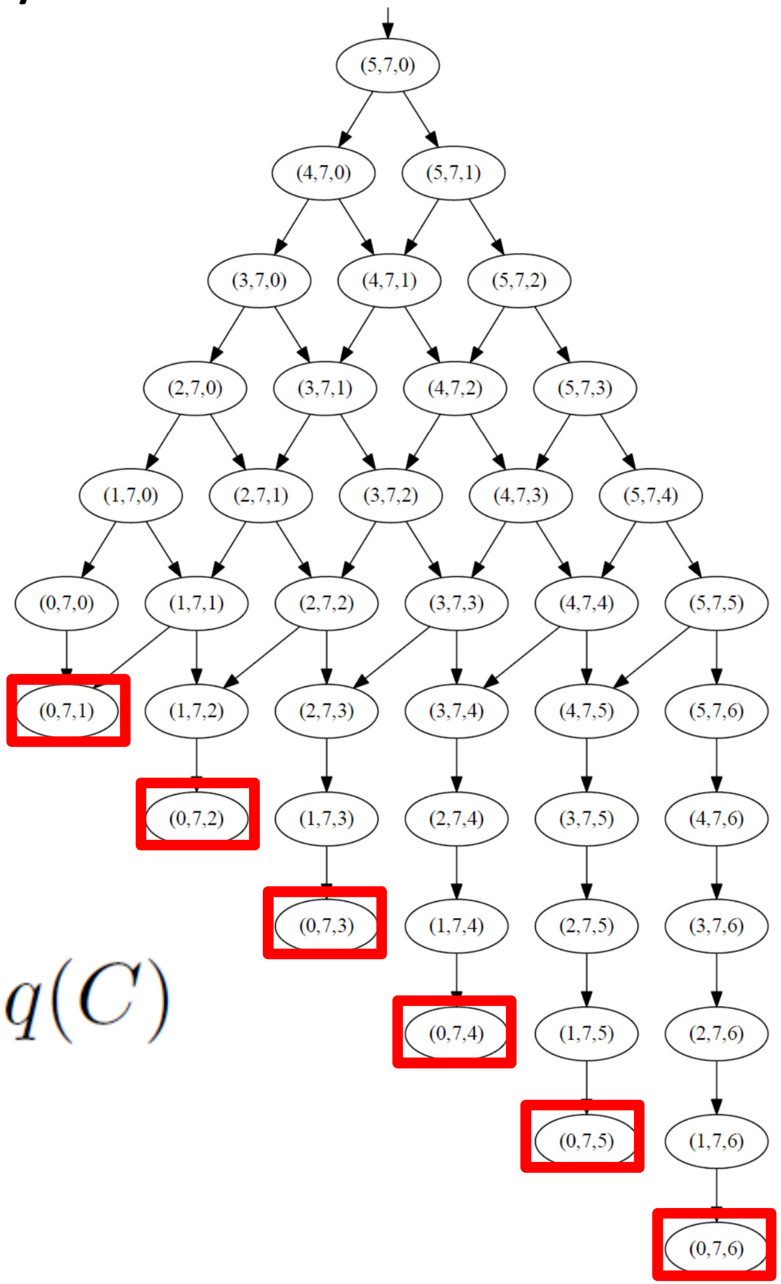
Application to the case study showing a race between unary and binary reactions

High level of A

$$A_T = 4\delta^7$$



$$q(B) \geq q(C)$$



Conclusion and prospects

- Setting of a formal and automatic method fo the derivation of an abstract semantics which accounts for the salient properties of our two case studies

- Prospects:
  - Identification of other refinements of the abstraction
  - Test on other case studies showing other properties of interest
  - Scaling up of the method

Thanks!